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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/348,354	07/07/1999	MENZO HAVENGA	4123US	5117

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EXAMINER	
LEFFERS JR, GERALD G	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 06/05/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/348,354	Applicant(s) HAVENGA ET AL.	
	Examin r Gerald Leffers	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *2/28/02* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,9-11 and 13-48* is/are pending in the application.

4a) Of the above claim(s) *13-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,9-11 and 33-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 July 1999* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *22,25* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt is acknowledged of applicants' amendment, filed 2/28/02 as Paper No. 24, in which claims were amended (claims 2-3) and new claims added (claims 33-42). It is noted that in the body of Paper No. 24 it is erroneously indicated that claims 1, 9 and 11 have been cancelled. These claims remain pending in the application.

Receipt is also acknowledged of a supplemental amendment, filed 3/6/02 as Paper No. 26, in which several claims were further amended (claims 2-3, 33, 35, 37 and 40). Claims 2-3, 9-11, 13-48 are pending in this application. Claims 13-32 have been withdrawn from consideration as being directed towards nonelected inventions.

Information Disclosure Statement

Receipt is acknowledged of two information disclosure statements, filed 2/28/02 and 3/6/02 as Papers No. 22 and 25, respectively. The corresponding PTO Form 1449 for each IDS has been signed and initialed and mailed with this action.

Claim Rejections - 35 USC § 102

(e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1, 9 and 11 are rejected under 35 U.S.C. 102(e) as being anticipated by Crystal et al (U.S. Patent No. 6,127,525). **This rejection is maintained for reasons of record in Papers No. 10, 14 and 20.**

Response to Arguments

In the body of the response in Paper No. 22, applicants' erroneously indicate that claims 1, 9 and 11 have been cancelled. The remaining claims rejected over Crystal et al, and new claims incorporating the limitations of claims 9 and 11, have been amended to include a limitation that the amino terminal region of the fiber from the adenovirus that the vector is derived from be fused to the tropism-determining region of the fiber from a second adenovirus of different serotype. Because claims 1, 9 and 11 have not been amended and have not actually been cancelled, the claims remain rejected as anticipated by Crystal et al for reasons of record.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2-3, 10 and 33-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crystal et al (U.S. Patent No. 6,127,525; see the entire document) in view of Wickham et al (U.S. Patent No. 5,770,442; see the entire patent). **This is a new rejection necessitated by applicants' amendment of the claims in Papers No. 24 and 26.**

Crystal et al teach a chimeric adenoviral coat protein (particularly a chimeric adenovirus hexon and/or fiber protein) with a decreased ability or inability to be recognized by a neutralizing antibody directed against the corresponding wild-type adenovirus coat protein for gene therapy (e.g. Abstract). Crystal et al further teach that the adenovirus coat proteins can be modified by deleting and replacing a region of the coat protein (e.g. a penton, hexon and/or fiber protein) with the corresponding region from another adenoviral serotype (e.g. Ad1, Ad3, Ad5, Ad6, Ad7, Ad8, Ad11, Ad12, Ad14, Ad16, Ad21, Ad34, Ad35, Ad40, Ad41 and Ad48). Crystal et al teach that a passenger gene such as therapeutic genes or reporter genes that can be carried on a plasmid vector and used in the construction of adenoviral gene transfer vectors for use in gene therapy (e.g. columns 14-16; Figures 1 and 2). Crystal et al teach a method of producing a chimeric adenovirus with a transfer vector such as an adenoviral vector (e.g. virions or virus particles) comprising a chimeric coat protein wherein a vector comprising sequences form the adenoviral left arm and a vector comprising sequences form the adenoviral right arm are introduced into a packaging cell (e.g. a 293 cell), generating a recombinant vector that comprises a portion of each of the vectors (column 18).

Although Crystal et al clearly anticipate making chimeric fiber proteins, Crystal et al do not explicitly teach the limitation of generating a fusion fiber protein wherein the amino-terminal region of the fiber adenovirus from which the adenoviral vector is derived is retained and operatively linked to the tropism-determining domain (e.g. the "knob" or c-terminal region) of the fiber from a second adenovirus of a different serotype.

Wickham et al teach the construction of adenoviral fiber proteins for use in altering the tropism of adenoviral vectors for gene therapy wherein the amino-terminal region of the adenovirus from which the vector is derived in retained and operatively linked to the tropism-determining domain of an adenovirus of a second serotype (e.g. column 5, lines 39-61; column 6, lines 29-52; column 8, lines 51-56; Examples 1 & 2; Figures 6 & 8). Wickham et al teach that one can advantageously practice the claimed invention by utilizing restriction enzyme sites within the native fiber coding sequence to incorporate various different nonnative receptor or protein binding domains into the chimeric fiber protein (e.g. Examples 1-2; column 7, lines 37-61).

It would have been obvious to one of ordinary skill in the art at the time of applicants' invention to practice the methods taught by Crystal et al for construction of adenoviral gene transfer vectors comprising a chimeric fiber and chimeric hexon with chimeric fibers comprising an amino terminal fiber region from a first serotype and a tropisms-determining domain (i.e. the "receptor-binding" domain according to Wickham et al) derived from an adenovirus of a different serotype because Crystal et al teach it is within the skill of the art to develop and use adenoviral constructs comprising chimeric hexon and fiber proteins and Wickham et al teach it is within the skill of the art to construct and use chimeric fiber proteins having a receptor binding

domain obtained from an adenovirus of a second serotype. One would have been motivated to do so in order to receive the expected benefit of being able to efficiently interchange different receptor-binding domains from adenoviruses of different serotype, as taught by Wickham et al, so as to easily and rapidly alter the tropism of the adenoviral vectors taught by Crystal et al. Absent any evidence to the contrary, there would have been a reasonable expectation of success in utilizing the teachings of Wickham et al and Crystal et al to generate recombinant adenoviral gene-transfer vectors comprising chimeric hexon and fiber proteins wherein the chimeric fiber protein comprises the amino-terminal region of the fiber and a c-terminal tropism-determining domain obtained from an adenovirus of different serotype.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-3, 10 and 33-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Each of the claims comprises a limitation wherein the part of the chimeric fiber obtained from an adenovirus of a second serotype is fused to the portion of the chimeric fiber derived from the first serotype from which the adenoviral vector is derived at its "N-terminus". The claims are vague and indefinite in that there is no clear definition provided in the specification as to what amino acids of the native adenoviral vector are considered to fall within the "N-terminus" of the native fiber for the adenovirus from which the vector is derived. Nor does the

specification appear to clearly indicate a functional limitation that defines the metes and bounds of the "N-terminus" of the chimeric fiber protein. It would be remedial to amend the claim language to clearly indicate the metes and bounds of the term "N-terminus".

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr.
Examiner
Art Unit 1636

ggl
June 3, 2002

DAVID GUZO
PRIMARY EXAMINER